SM

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/941,193	08/28/2001	James E. Dahlberg	FORS-06613	6777

23535 7590 04/20/2004

MEDLEN & CARROLL, LLP
101 HOWARD STREET
SUITE 350
SAN FRANCISCO, CA 94105

EXAMINER	
AKHAVAN, RAMIN	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 04/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Appt 04/19/04 RA

Office Action Summary	Application No.	Applicant(s)	
	09/941,193	DAHLBERG ET AL.	
	Examiner	Art Unit	
	Ramin (Ray) Akhavan	1636	

818

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 August 2001*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *95-108* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *95-108* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Applicant's preliminary amendment of this application is acknowledged, filed August 21, 2001, where claims 45-94 and 109-123 were cancelled. In addition, it is acknowledged that the specification was amended to include reference to prior applications. The pending claims are claims 95-108.

Priority

Applicant's claim for priority is based on multiple applications dating as far back as 12/04/1992 (Application No. 07/986,330, US 5,422,253). However, base claim 95 is drawn to a system comprising a target nucleic acid, first, second and third oligonucleotide. There does not appear to be any support for such a system in the '330 application. However, there does appear to be support for such a system in Application No. 08/073,384, filed 06/04/1993 (US 5,541,311). Therefore, claims 95-96 and 99-108 are granted a **priority date of 06/04/1993**.

Claims drawn to a fluorophore label (Claims 97-99) find support beginning with Application No. 08/254,359 (US 5,614,402) filed 06/06/1994, therefore, claims 97-99 are granted a priority date of 06/06/1994.

Specification

The use of the trademarks Cleavase, CFLP, Oligotex and QIAamp has been noted in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

Claim Objections

Claim 107 is objected to because of the following informalities: The claim recites the phrase, "wherein said portion said third oligonucleotide..." The phrase would be more intelligible with the term "of" placed in between the terms "portion" and "said". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

1. **Claim 95-108 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.**

The claims recite the term "system". There does not appear to be a specific definition for this term in the specification. It is unclear whether "system" is to be interpreted to mean that the claims are drawn to specific method steps or the claims are drawn to a way of using a particular product, or simply to a composition (e.g. a kit) comprising the recited nucleic acids. Therefore, the claims' metes and bounds are indefinite. For example, in claims drawn to a method comprising a number of action steps, there would eventually a particular outcome. The instant claims are so vague and indefinite, that it is unclear what outcome is intended.

Claim 95 recites the limitation "said at least a portion" in referring to "said third oligonucleotide". There is insufficient antecedent basis for this limitation in the claim. The only reference in the claim to "at least a portion" is to the second oligonucleotide.

Claims 97-99 recite the limitation "said label". There is insufficient antecedent basis for this limitation in the claim, since the claims are dependant from claim 95, which makes no reference to a "label".

Claim 107 recites the limitation "said portion", when referring to "said third oligonucleotide". There is insufficient antecedent basis for this limitation in the claim. The claim ultimately depends from Claim 95, which does not recite portion in any way in reference to a third oligonucleotide.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

2. **Claims 95-100, 102, 104 and 105 are rejected under 35 U.S.C. 102(b) as being anticipated by Lundeberg et al. (DNA Cell Bio. 1990; 9(4):287-92; see entire document).**

The claims are broadly drawn to a system comprising a target nucleic acid having a first and second region, a first oligonucleotide, a second oligonucleotide, a third oligonucleotide and wherein at least the 3' portion of the first oligonucleotide is complementary to said first region of the target and at least a portion of the second oligonucleotide is complementary to the second region of the target nucleic acid and wherein the 5' portion of the first oligonucleotide is complementary to at least a portion of said third oligonucleotide. In addition the second oligonucleotide is attached to a solid support, the first and second portions of the target nucleic acid are adjacent and the second oligonucleotide comprises a 3' terminus.

Lundeberg et al teach a colorimetric assay to detect immobilized nucleic acids. More particularly, the assay involves three oligonucleotides, with two having complementary sequences to 5' and 3' portions of a target nucleic acid and a third labeled oligonucleotide that has complementary sequence to one of the preceding oligonucleotides. (e.g. p. 288, Fig. 1). In addition, Lundeberg et al teach that two of the oligonucleotides comprise a biotin and fluroescein label. (e.g. p. 288, col. 2, ¶ 2). Furthermore, the oligonucleotide priming at the 3' portion of the target nucleic acid is attached to a solid support, i.e. oligonucleotide comprising the *lac* operon sequence bound to sepharose. (e.g. p. 289, col. 1, ¶ 2).

In addition, the second oligonucleotide – as with any oligonucleotide – necessarily has a 3' terminus. Furthermore, as the term adjacent is interpreted as broadly as reasonable, a target nucleic acid region that is 5' of another region would be adjacent relative to the other region. Therefore, Lundeberg et al anticipates the rejected claims.

3. **Claims 95-96 and 99-104 are rejected under 35 U.S.C. 102(e) as being anticipated by Yamamoto et al. (US 5,830,643; hereinafter '643 patent; see entire document).**

The '643 patent teaches a method of detecting a target nucleic acid comprising a first, second and third oligonucleotide. (e.g. col. 6, ll. 30-45). In addition, any of the oligonucleotides can be labeled. (e.g. col. 6, l. 65). The labeling substance can be, a radioisotope or a non-radioactive substance such as biotin. (e.g. Col. 11, ll. 4-10). Furthermore, any of the oligonucleotides can be immobilized onto a solid support (i.e. carrier). (e.g. col. 4, ll. 20-40). The oligonucleotides produced are intended for use as probes for detection of a target nucleic acid (e.g. such as a gene). (e.g. col. 1, ll. 18-20). Therefore, the '643 patent anticipates the rejected claims.

4. **Claims 95-96 are rejected under 35 U.S.C. 102(e) as being anticipated by Takarada et al. (US 5,525,462; hereinafter '462 patent; see whole document).**

The '462 patent teaches a method of detecting a target nucleic acid comprising three oligonucleotides, with one having sequences complementary to a 5' region of the target, another oligonucleotide having sequences complementary to a 3' region of the target nucleic acid and a third oligonucleotide comprising sequences complementary to the preceding oligonucleotide. (e.g. col. 10, ll. 26-32; col. 12, ll. 1-25). In addition, either of the target specific or oligo-specific oligonucleotides comprises a label. (e.g. col. 9, ll. 63-65; col. 12, ll. 13-17). Therefore, the '462 patent anticipates the rejected claims.

Claim Rejections - 35 USC § 103

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the

various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 95-104 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yamamoto et al. (US 5,830,643; hereinafter '643 patent, further in view of Stavrianopoulos (US 5,989,809; hereinafter '809 patent).

The claims are drawn to a system comprising three oligonucleotides, wherein a target nucleic acid has two regions, wherein the first oligonucleotide is complementary to one region, the second oligonucleotide is complementary to the second region and the third oligonucleotide is complementary at least in part to the first oligonucleotide. Additional claims are drawn to one of these oligonucleotides comprising a fluorophore label.

The '643 patent teaches a method of detecting a target nucleic acid comprising a first, second and third oligonucleotide. (e.g. col. 6, ll. 30-45). In addition, any of the oligonucleotides can be labeled. (e.g. col. 6, l. 65). The labeling substance can be, a radioisotope or a non-radioactive substance such as biotin. (e.g. Col. 11, ll. 4-10).

Furthermore, any of the oligonucleotides can be immobilized onto a solid support (i.e. carrier). (e.g. col. 4, ll. 20-40). The oligonucleotides produced are intended for use as probes for detection of a target nucleic acid (e.g. such as a gene). (e.g. col. 1, ll. 18-20).

The '643 patent does not specifically teach that the label can be fluorophores or fluorophores having quenched emission.

The '809 patent teaches a method for detecting a presence of a target polynucleotide comprising hybridizing an oligonucleotide to a target nucleic acid. Generally, the '809 method comprises use of fluorophore emissions quenching as a means of detecting nucleic acids, where the nucleic acids to be detected are attached to a solid support (e.g. Abstract; columns 2-5; col. 5, ll. 45-55; col. 7, ll. 55-60). The method is useful for facilitating isolation and detection of a nucleic acid involving hybridization. (e.g. col. 7, ll. 27-45).

It would have been obvious to one of ordinary skill in the art at the time of filing of instant application to combine the teachings of the '643 patent with the '809 patent in a method of hybridization using nucleic acids where one of the nucleic acids is labeled with a fluorophore. The skilled artisan would have been motivated to modify the oligonucleotides with fluorophore labels to achieve the advantageous and beneficial use of fluorescence quenching and immobilization to a solid support to facilitate hybridization/detection. Furthermore, the skilled artisan would have had a reasonable expectation of success in modifying hybridizing oligonucleotides in this fashion.

6. Claims 95-99 are rejected under 35 U.S.C. 103(a) as being unpatentable over Takarada et al. (US 5,525,462; hereinafter '462 patent, further in view of Stavrianopoulos (US 5,989,809; hereinafter '809 patent).

The '462 patent teaches a method of detecting a target nucleic acid comprising three oligonucleotides, with one having sequences complementary to a 5' region of the target, another oligonucleotide having sequences complementary to a 3' region of the target nucleic acid and a third oligonucleotide comprising sequences complementary to the preceding oligonucleotide. (e.g. col. 10, ll. 26-32; col. 12, ll. 1-25). In addition, either of the target specific or oligo-specific oligonucleotides comprises a label. (e.g. col. 9, ll. 63-65; col. 12, ll. 13-17).

The '462 patent does not teach that the label can be fluorophores or fluorophores having quenched emission.

As discussed above, the '809 patent teaches attaching a fluorophore label to oligonucleotides in a method of hybridization/detection.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ray Akhavan whose telephone number is 571-272-0766. The examiner can normally be reached on Monday- Friday from 8:00-4:30. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy

Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

GERRY LEFFERS
PRIMARY EXAMINER